


PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1255WOORD01	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/EP2005/050708	International filing date (day/month/year) 17.02.2005	Priority date (day/month/year) 18.02.2004	
International Patent Classification (IPC) or national classification and IPC INV. C07D221/12 A61K31/473 A61P11/00 A61P29/00 A61P37/02			
Applicant ALTANA PHARMA AG et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 13.12.2005		Date of completion of this report 26.05.2006	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Traegler-Goedel, M Telephone No. +49 89 2399-8278	



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2005/050708

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-56 as originally filed

Claims, Numbers

1-14 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2005/050708

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 13,14

because:

☒ the said international application, or the said claims Nos. 13,14 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*).

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b) and 13ter.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2005/050708

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-14
Industrial applicability (IA)	Yes: Claims	1-12
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

see separate sheet

re item III:

Claims 13 and 14 have to be considered as being directed to the treatment of the human and/or animal body. Under the terms of Rule 67.1 and Art. 34 (4)a)i PCT the International Preliminary Examination Authority is not required to carry out an examination on such claims.

re item V:

1. Prior art

The examining procedure is based on the documents cited in the International Search Report:

- D1: WO 2004/018431 A (WEINBRENNER STEFFEN ; SCHMIDT BEATE (DE); ALTANA PHARMA AG (DE); FLOCK) 4 March 2004 (2004-03-04)
- D2: WO 02/066476 A (BYK GULDEN LOMBERG CHEM FAB ; FLOCKERZI DIETER (DE)) 29 August 2002 (2002-08-29)
- D3: US-B-6 306 869 B1 (FLOCKERZI DIETER) 23 October 2001 (2001-10-23)
- D4: US-B-6 476 025 B1 (GUTTERER BEATE) 5 November 2002 (2002-11-05)

2. Novelty

The present 6-(urea substituted)phenylphenanthridine derivatives differ from those according to D1 by the substituents R⁴ and R⁵ (being either a group -OR₄₁ or -O-R₅₁ instead of hydrogen or alkyl) and are distinguished from the 6-(urea substituted)-phenylnaphthyridine derivatives according to D2 and D3 by the replacement of a nitrogen by a carbon atom in the tricyclic moiety and from the 6-(substituted)-phenylnaphthyridine derivatives according to D3 additionally by the urea group instead of an amide group as substituent of the phenyl residue in position 6. The present compounds differ structurally from the 6-(substituted)phenylphenanthridine derivatives according to D4 only by the urea group instead of an amide group as substituent of the phenyl residue in position 6. Thus the subject matter of claims 1 to 14 is considered to fulfil the requirements of Art. 33 (2) PCT with respect to documents D1 to D4.

3. Inventive step

Documents D2 and D3 are concerned with 6-(substituted)phenylnaphthyridine derivatives and D4 is concerned with 6-(substituted)phenylphenanthridine derivatives which all are potent inhibitors of phosphodiesterase (PDE) IV as are the 6-(substituted)phenylphenanthridine derivatives of the present application. The naphthyridines of D3 and the phenanthridines of D4 have the same substituents in the phenyl residue in position 6, inter alia amides. The structural closest prior art showing the at least qualitatively the same pharmacological activity is to be seen in document D2, since these compounds, bearing also the essential urea substituent in the phenyl group in position 6 differ merely by the naphthyridine instead of the phenanthridine residue, i.e. a nitrogen has been replaced by a carbon in the present compounds.

If the problem underlying the present application were to be seen in provision of further PDE IV inhibitors, the solution of the problem must be considered as being obvious for the following reason:

From the relevant prior art documents D3 and D4 it was known that the replacement of the tricyclic naphthyridine moiety (D3) by the tricyclic phenanthridine moiety (D4) both substituted in the phenyl residue in position 6 by an amide does not change the PDE IV inhibitory activity, since both types of compounds are potent inhibitors of PDE IV. Thus it was completely obvious for the skilled person to try this exchange with 6-(urea substituted)phenylnaphthyridines as known from D2 as well to result with the claimed 6-(urea substituted)phenyl phenanthridine derivatives.

Therefore, re that very close prior art (structurally and concerning activity), the problem underlying the present application, the solution of which could involve an inventive step, is therefore to be seen in the provision of compounds that exhibit an unexpected or surprising effect as compared to the structural closest prior art compounds according D2. The Applicant's attention is drawn to the fact, that any comparative tests should be made with compounds of the closest prior art, showing the closest possible structural similarity, differing structurally only in the essential feature, i.e. only in the feature which renders the

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2005/050708

subject matter novel and which an inventive step may be based on. If such an effect could be demonstrated (preferably by concrete experimental data) an inventive step might be acknowledged at least for the specified or exemplified compounds of the present application. And, in this case the breadth of the claims appears to be acceptable since in principle known from the closest prior art D2. Thus, the subject matter of claim 1 and the dependent ones does not fulfil the requirements of Art. 33 (3) PCT.

4. Industrial applicability

No objection arises with respect to claims 1-12, since the claimed compounds may be used for the production of pharmaceutical compositions.

re item VI:

It is brought to the Applicant's attention, that the part of document D1 as cited above and entitled to its EP priority if entering the European phase, were relevant for the consideration of inventive step.